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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte LARRY CALDWELL,
BRADLEY S. GALER, and LAWRENCE NEWMAN

Appeal 2010-000947
Application 10/029,407
Technology Center 1600

Before DONALD E. ADAMS, LORA M. GREEN, and
STEPHEN WALSH, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This is a decision on appeal under 35 U.S.C. § 134 from the Examiner's rejection of claims 1-18 and 24-33. We have jurisdiction under 35 U.S.C. § 6(b).

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

STATEMENT OF THE CASE

Claim 1 is representative of the claims on appeal, and reads as follows:

1. A method for ameliorating headache pain caused by a tension headache, migraine headache, indomethacin responsive headache syndrome or cluster headache, said method consisting of

topically applying an anti-inflammatory effective amount of a topical NSAID formulation comprising an NSAID as the only active agent present in said topical formulation to a keratinized skin surface of the head of said host to ameliorate said headache pain caused by a tension headache, migraine headache, indomethacin responsive headache syndrome or cluster headache.

The following ground of rejection is before us for review:

Claims 1-18 and 24-33 stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by the combination of either Pradalier[2] or Cluff,[3] as combined with Caldwell[4] and Toppo.[5]

We affirm.

ISSUE

Has the Examiner established by a preponderance of the evidence that the combination of references renders obvious the claimed methods?

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[2] A. Pradalier and D. Vincent, *Migraine and non-steroidal anti-inflammatory agents*, 40 PATHOL BIOL. 397-405 (1992).
[3] Robert S. Cluff, *Migraine Treatment*, International Association for the Study of Pain Technical Corner from IASP Newsletter, 1999.
[4] Caldwell et al., US 5,667,799, Sept. 16, 1997.
[5] Toppo, US 5,318,960, June 7, 1994.

FINDINGS OF FACT

FF1 According to the Specification, the invention is drawn to "the treatment of headache pain" (Spec. 1).

FF2 According to the Specification:

> A variety of therapeutic agents have been developed for use in the treatment of patients suffering from headache pain. Some agents, such as aspirin, acetaminophen, vasoconstrictors and NSAIDs, e.g. ibuprofen and naprosyn, are administered systemically. Despite the prevalence of this form of treatment for headache pain, in some cases, systemic administration is not recommended. For example, oral administration of aspirin can result in stomach upset and patient discomfort. Furthermore, the agent can exert host systemic toxicity which may outweigh any therapeutic benefits provided by the agent. Finally, since the agent is administered systemically, its effects are also systemic, which may not be desired.

(*Id.*)

FF3 The Specification teaches methods of applying "a topical NSAID formulation . . . to a keratinized skin site proximal to the pain associated with the headache pain, e.g., a keratinized skin surface of the head, such as the forehead, temple, occipital region, etc." (*Id.* at 2).

FF4 The Specification teaches further that "[p]ractice of the subject methods results in at least a reduction in the intensity of the pain associated with the headache" (*id.*).

FF5 The Specification also teaches that "[i]n practicing the subject methods, the topical NSAID formulation is applied to a keratinized skin surface of the host in a manner sufficient to provide for penetration of an affective amount of the NSAID to the nerves and soft tissues, muscles,

tendons, ligaments, etc., causing the pain associated with the syndrome being treated" (*id.* at 5).

FF6 The Specification teaches further:

> In certain embodiments of the subject methods, the topical composition comprising the NSAID is applied to a keratinized skin site of the host proximal to target nerves associated with the headache pain. Nerves which are commonly associated with headache pain are the occipital and supraorbital nerves. The skin site at which the composition is applied will be sufficiently proximal to the target nerves, e.g., the skin site overlies the region innervated by the target nerves, so that upon contact of the composition with the skin surface, the NSAID active agent can readily reach the target nerves (and/or muscles of the forehead, temples and occipital regions) and exert its anti-inflammatory activity. Of particular interest as skin sites of topical application are the supraorbital and occipital regions.

(*Id.* at 6.)

FF7 Thus, according to the Specification, "[u]pon application of the topical composition, the NSAID present therein penetrates the surface of the skin to reach the pain origin and reduce at least one symptom associated with the syndrome being treated" (*id.* at 7).

FF8 The Specification also teaches:

> The above described invention finds use in treating a host suffering from a headache, i.e., from a pain in the head, cephalalgia, headache pain. The headache may be any of a variety of different types of headaches, including but not limited to: tension headache, migraine headache, cluster headache, headache associated with inflamed sinuses, temporal arteritis, or other causes.

(*Id.* at 8.)

FF9 The Examiner's statement of the rejection may be found at pages 3-6 of the Answer.

FF10 The Examiner cites Pradalier and Cluff for teaching the use of NSAIDs in the treatment of migraine (Ans. 4).

FF11 The Examiner notes that neither Pradalier nor Cluff teaches the topical administration of the NSAID (*id.*).

FF12 The Examiner cites Toppo for teaching a composition comprising an NSAID for pain relief, wherein the composition may be applied topically (*id.*). The NSAIDs include indomethacin, ketoprofen, diclofenac, and ibuprofen (*id.*).

FF13 The Examiner further finds that Toppo teaches that topical administration allows the NSAID to be delivered precisely to the body at a specific area of pain, alleviating the side effects that may occur with systemic administration (*id*).

FF14 In addition, Toppo teaches that the composition "has the capacity to affect the individual surface skin cells (corneocytes) and allow the passage of medicaments to sub-dermal afflicted areas deep within the skin" (Toppo, Abstract).

FF15 Toppo states that the disclosed invention "relates to a composition, and method of manufacture thereof, for transdermal delivery of pain relieving substances directly to afflicted areas of the body" (Toppo, col. 1, ll. 6-9).

FF16 In the "Description of the Prior Art," Toppo also discusses the issues related to the treatment of arthritis (*id.* at col. 1, ll. 13-34).

FF17 The Examiner finds that Caldwell teaches a "method for treatment of host suffering from headache pain with topical application of local anesthetic applied to keratinized skin proximal to target nerves associated with the headache pain, usually to the supraorbital or occipital regions of the head, so the drug penetrates the skin to block conduction in the target nerves and provides pain relief to the host" (Ans. 4).

FF18 The Examiner concludes that it would have been obvious to use the topical NSAID formulation taught by Toppo to treat headaches such as migraine headaches because Pradalier and Cluff teach the use of NSAIDs for the treatment of such headaches (*id.* at 5-6).

FF19 The Examiner further concludes:

> In view of the state of the art, a person skilled in the art at the time of the invention aware of side effects caused by NSAIDs when given orally, and aware of their suitability for topical application to act locally without systemic effect, it is no difficult task for such a skilled artisan to deliver NSAIDs topically at the site of pain to obtain relief without gastrointestinal unwanted side effects.

(*Id.* at 8.)

FF20 As to claims 29 and 30, the Examiner concludes that it would have been well within the level of skill of the ordinary artisan to optimize the dosage required (*id.* at 22).

FF21 The Declaration of Dr. Lawrence C. Newman, dated December 9, 2002 (attached to the Appeal Brief), states that before the instant invention, "there was an extremely low expectation of success that a topical formulation of indomethacin could supply a therapeutically effective amount of indomethacin to successfully treat indomethacin-responsive headaches."

PRINCIPLES OF LAW

During prosecution before the Office, claims are to be given their broadest reasonable interpretation consistent with the Specification as it would be interpreted by one of ordinary skill in the art. *In re American Academy Of Science Tech Center*, 367 F.3d 1359, 1364 (Fed. Cir. 2004). "An essential purpose of patent examination is to fashion claims that are precise, clear, correct, and unambiguous. Only in this way can uncertainties of claim scope be removed, as much as possible, during the administrative process." *In re Zletz*, 893 F.2d 319, 322 (Fed. Cir. 1989).

The Supreme Court has emphasized that "the [obviousness] analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007). "If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. (*Id.* at 417.) Under the correct obviousness analysis, "any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed." *Id.* at 420.

ANALYSIS

Claim 1 is drawn to a "method for ameliorating headache pain caused by a tension headache, migraine headache, indomethacin responsive headache syndrome or cluster headache." In view of the Specification, we interpret that as only requiring the reduction of pain associated at least one

symptom associated with the syndrome being treated (*see* FFs 4 and 7). Thus, the claim does not require treatment of the cause of the headache, but only a reduction in the amount of pain associated with any of the symptoms associated with the headache. That encompasses topical application for the treatment of nerves and soft tissues, muscles, tendons, ligaments, etc., causing the pain associated with the syndrome being treated (FF5), as well as the topical application to the supraorbital and occipital regions of the head, which are proximal to the occipital and supraorbital nerves (FF6). We now turn to Appellants' arguments.

Appellants argue with respect to the claims in Group I (claims 1-18, 24-26, 28, 32, and 33 (App. Br. 5), of which we choose claim 1 as representative), that the claims are drawn to treating headaches that are caused by disturbances in the central nervous system, and thus the claims require applying a topical medicament to a skin site which is not the site of origin of the pain, that is, the brain (*id.* at 7-8). Appellants further assert that "[i]t is known by those of ordinary skill in the art that topically applied formulations do not result in clinically significant systemic blood levels, and do not produce any significant systemic side effects" (*id.*).

Appellants assert that Pradalier and Cluff are drawn to oral administration of NSAIDs for the treatment of migraine, which is well known in the art (*id.* at 9). Toppo, Appellants argue, is drawn to the use of NSAIDS for pain, but that the only pain mentioned is arthritis pain, and thus "the area of pain experienced is also the exact site of inflammation and pain generation, causing the symptom of pain in the exact same body region" (*id.*). Caldwell, Appellants assert, "is directed to a pain relief composition

whose active agent is a local anesthetic and with distinct and different specified areas of drug application," and the ordinary artisan "would not extrapolate using the locally-applied nerve-blocking agent in Caldwell to the teaching of the other references to topically apply NSAID for treatment of central headaches as in the current claims" (*id.* at 9-10). Appellants thus assert that the references relied upon by the Examiner do not teach or suggest "topically applying a topical NSAID formulation to a keratinized skin surface of the head to treat a headache of central nervous system origin, as claimed" (*id.* at 10). Appellants argue further that the Examiner has relied upon improper hindsight in combining the references (*id.* at 11).

> Appellants argue further that the ordinary artisan
>
> would not have had a reasonable expectation of success in using a topical formulation of an NSAID applied to the keratinized skin surface of the head because (1) it was believed that the underlying pathophysiologic mechanism of migraines, indomethacin-responsive headaches, tension headaches, and cluster headaches were related to abnormalities deep within the brain; (2) it was known that topical formulations act locally and do not produce any significant drug levels in the systemic circulation nor in the brain; and (3) oral NSAIDs were known to successfully treat headache symptoms only if clinically significant systemic blood levels were achieved, as supported by the declaration provided by Dr. Newman.

(*Id.* at 10-11.)

Appellants' arguments have been carefully considered, but are not convincing. First, Appellants argue that the claims require treatment of the central nervous system as the origin of a tension headache, migraine headache, indomethacin responsive headache syndrome or cluster headache, but as discussed above in the claim interpretation, treatment of the nervous

system by topical application of the NSAID formulation is not required by the claim. The claims encompass any reduction of pain of any symptom associated with those headaches, and as taught by the instant Specification, that can be accomplished by topically applying the NSAID formulation to the keratinized skin surface of the head to treat the nerves and soft tissues, muscles, tendons, ligaments, etc., which may be reached by the topical application of the NSAID.

Moreover, we agree with the Examiner that the combination of Pradalier or Cluff, as combined with Caldwell and Toppo, renders the method of claim 1 obvious. Pradalier and Cluff teach that headaches such as migraine headaches may be treated with NSAIDs. Toppo teaches a topical formulation of an NSAID for the treatment of pain, wherein the composition has the capacity to affect the individual surface skin cells and allow the passage of medicaments to sub-dermal afflicted areas deep within the skin (FF14). Caldwell demonstrates that headache pain may be treated topically. Thus, given the complications associated with the systemic administration of NSAIDs, the combination of references would suggest a method of topically applying an NSAID formulation for the reduction of any pain associated with tension headache, migraine headache, indomethacin responsive headache syndrome or cluster headache. Note that all that is required is a reasonable expectation of success, not absolute predictability of success. *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988).

As to Appellants' arguments regarding Toppo, while Toppo only specifically discusses arthritis pain, it talks about pain generally, and it would be well within the level of skill of the ordinary artisan to use the

formulation of Toppo to treat pain associated with sub-dermal afflicted areas deep within the skin. We have also considered Appellants' arguments that Caldwell is drawn to administration of a nerve-blocking agent, but the ordinary artisan would understand that pain can be treated using various known agents, such as the NSAIDs taught by Toppo. Similarly, we do not find the Declaration of Dr. Newman persuasive as the claims do not require treatment of the cause of indomethacin-responsive headaches, but only a reduction in pain that may be associated with such a headache.

As to claim 27, Appellants argue that none of the references relied upon by the Examiner teach or suggest "a method of treating headache pain from an Indomethacin Responsive Headache Syndrome by topically applying a topical NSAlD formulation comprising an NSAlD as the only active agent present in the topical formulation to a keratinized skin surface of the head of the host" (App. Br. 13). Appellants also reiterate the arguments made with respect to claim 1 (*see id.* at 13-14).

Appellants' arguments have been considered, but are not found to be convincing for the reasons set forth above. In addition, the ordinary artisan would expect a topical NSAID formulation to be useful to treat pain associated with any headache, including Indomethacin Responsive Headache Syndrome.

As to claims 29 and 30, Appellants again reiterate the arguments made with respect to claim 1 (App. Br. 14-15). Appellants argue further that the claims specify the amount of NSAID in the topical formulation, and the Examiner "has provided no valid apparent reason" for the rejection of those claims (*id.* at 15).

Again, Appellants' arguments are not persuasive for the reasons set forth above. Also, we agree with the Examiner that it would have been well within the level of skill of the ordinary artisan to optimize the dosage amounts of the NSAID in the topical formulation. *See In re Boesch*, 617 F.2d 272, 276 (CCPA 1980) (noting that determining the optimum values of result effective variables is ordinarily within the skill of the art).

As to claim 31, Appellants reiterate the arguments made with respect to claim 1 (App. Br. 16-17). Appellants argue further that claim 31 requires that the method results in no toxic side effects, but that the Examiner "has provided no valid apparent reason" for the rejection of those claims (*id.* at 16).

Appellants' arguments are again not found to be convincing for the reasons set forth above. In addition, as noted by the Examiner (Ans. 23), Pradelier and Toppo both recognized the problems associated with the systemic administration of NSAIDs, and Toppo specifically teaches the advantages of topical administration, such as reduction of the side effects seen with systemic administration.

CONCLUSION OF LAW

We conclude that the Examiner has established by a preponderance of the evidence that the combination of references renders obvious the claimed methods. We thus affirm the rejection of claims 1-18 and 24-33 under 35 U.S.C. § 103(a) as being rendered obvious by the combination of either Pradalier or Cluff, as combined with Caldwell and Toppo.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

cdc

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